1999; Langeland *et al.*, 1999). This has been demonstrated for NAC (Llobert *et al.*, 1988; Banner *et al.*, 1986; Brumas *et al.*, 1992), captopril (Prontera *et al.*, 1999; Volpert *et al.*, 1996), amifostine (Polla *et al.*, 1990; Hirschel-Scholz *et al.*, 1988), and cystamine (McDonnell *et al.*, 1997). Both NAC (Dorr, 1998; Albini *et al.*, 1995) and captopril (Prontera *et al.*, 1999; Volpert *et al.*, 1996) have been reported to be effective in inhibiting zinc-dependent MMPs, which can be reversed by the addition of $ZnCL_2$ to the culture medium (Volpert *et al.*, 1996).

To extend these observations, amifostine's free thio form (WR-1065) has been evaluated, along with captopril and NAC, with regard to their abilities to inhibit MMPs secreted by human glioma cells. These data are presented in FIG. 3-5). WR-1065 at a concentration of 40 μM reduced MMP-2 activity by 45% and MMP-9 by 5% relative to matched controls. A 4 mM concentration of WR-1065 was equally as effective as the well characterized chelating agent EDTA in completely inhibiting both MMP-2 and MMP-9 activity. NAC both the D- and L-isomers, at a concentration of 10 mM inhibited MMP-2 by at least 69%. MMP-9 activity was also inhibited to a similar extent by both isoforms of NAC. Captopril at 10 mM concentration, completely inhibited the activity of both MMPs.

More specifically, the ability of WR-1065 to affect the activities of matrix metalloproteinase-2 (MMP-2) and-9 (MMP-9) in a human glioma cell line is demonstrated in FIG. 3. The effects of L-NAC, D-NAC and captopril are also presented in FIG. 4, and the results of the densimetric scanning of the gels are presented in FIG. 5. Briefly, following a 24 h exposure to a 40 μM concentration of WR-1065 (SH), MMP-2 activity was reduced to 55% of control levels. TNFα exposure, used as a positive control, at 10ng/ml was equally effective. The combination of the two agents did not enhance the inhibitory effect (see FIG. 6 ~~and FIG. 8~~). For MMP-9, 40 μM SH reduced activity by only 5%, but in contrast, TNFα enhanced it by about 85%. When concentrations of 4mM WR-1065 (SH), and 10 mM of L-NAC, D-NAC, or captopril were evaluated, SH and captopril completely inhibited both MMP-2 and MMP-9

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